CLAIMS

[1] A method for assessing the risk of drug-induced granulocytopenia, the method comprising detecting a polymorphism of the human insulin receptor substrate-2 gene of a subject, and determining the presence of the risk of drug-induced granulocytopenia of a subject by use of the genetic polymorphism as an index.

[2] A method of detecting a polymorphism of the human insulin receptor substrate-2 gene for determining the presence of the risk of drug-induced granulocytopenia of the subject, in which the genetic polymorphism is employed as an index.

[3] An examination method for the risk of drug-induced granulocytopenia, comprising detecting a polymorphism of the human insulin receptor substrate-2 gene of a subject, and carrying out an examination using the genetic polymorphism as an index for determination of the risk.

[4] A method as described in any of claims 1 through 3, wherein the presence of the risk of drug-induced granulocytopeniais determined by use, as an index, of at least one genetic polymorphism selected from the group consisting of human insulin receptor substrate-2 described below in (a) through (f):

(a) a polymorphism that is C (wild type) to A conversion at position 4,587 upstream of the translation initiation codon;

(b) a polymorphism that is AT (wild type) deletion at position 2,510 upstream of the translation initiation codon;

(c) a polymorphism that is A (wild type) to C conversion at position 1,164 upstream of the translation initiation codon;

(d) a polymorphism that is A (wild type) to G conversion at position 15,870 downstream from the translation initiation codon;

(e) a polymorphism that is A (wild type) to G conversion at position 29,793 downstream from the translation initiation codon; and

(f) a polymorphism that is C (wild type) deletion at position 31,532 downstream from the translation initiation codon;

[5] A method as described in any of claims 1 through 4, wherein the genetic polymorphism is detected through at least one technique selected from the group consisting of direct nucleotide sequencing, allele-specific oligonucleotide (ASO)-dot blot analysis, single nucleotide primer extension assay, PCR-single strand conformation polymorphism (SSCP) analysis, PCR-restriction enzyme fragment length polymorphism (RFLP) analysis, Invader assay, quantitative real-time PCR assay, and genetic polymorphism assay employing a mass spectrometer (mass array).

[6] A method as described in claim 5, wherein the genetic polymorphism is detected through direct nucleotide sequencing.

[7] A method as described in claim 5, wherein the genetic polymorphism is detected through PCR-restriction enzyme fragment length polymorphism (RFLP) analysis.

[8] A method as described in claim 7, wherein the PCR-restriction enzyme fragment length polymorphism (RFLP) analysis is performed by use of the restriction enzyme *Afa* I for detecting A to G conversion at position 29,793 downstream from the translation initiation codon of the human insulin receptor substrate-2 gene.

[9] An oligonucleotidewhich can be hybridized with the human insulin receptor substrate-2 gene is employed as a primer or probe for genetic polymorphism detection, the oligonucleotide being selected from the group consisting of oligonucleotides described below in (a) through (f):

(a) an oligonucleotide having a sequence including a genetic polymorphism that is C to A conversion at position 4,587 upstream of the translation initiation codon of the human insulin receptor substrate-2 gene;

(b) an oligonucleotide having a sequence including a genetic polymorphism that is AT deletion at position 2,510 upstream of the translation initiation codon of the human insulin receptor substrate-2 gene;

(c) an oligonucleotide having a sequence including a gene polymorphism that is A to C conversion at position 1,164 upstream of the translation initiation codon of the human insulin receptor substrate-2 gene;

(d) an oligonucleotide having a sequence including a gene polymorphism that is A to G conversion at position 15,870 downstream from the translation initiation codon of the human insulin receptor substrate-2 gene;

(e) an oligonucleotide having a sequence including a gene polymorphism that is A to G conversion at position 29,793 downstream from the translation initiation codon of the human insulin receptor substrate-2 gene; and

(f) an oligonucleotide having a sequence including a genetic polymorphism that is C deletion at position 31,532 downstream from

the translation initiation codon of the human insulin receptor substrate-2 gene.

[10] An oligonucleotidewhich can be hybridized with the human insulin receptor substrate-2 gene is employed as a primer for genetic polymorphism detection, the oligonucleotide being selected from the group consisting of oligonucleotides described below in (a) through (d) and (f):

(a) an oligonucleotide having the sequence of SEQ ID NO: 3;

(b) an oligonucleotide having the sequence of SEQ ID NO: 6;

(c) an oligonucleotide having the sequence of SEQ ID NO: 9;

(d) an oligonucleotide having the sequence of SEQ ID NO: 12; and

(f) an oligonucleotide having the sequence of SEQ ID NO: 17.

[11] A kit for assessing the risk of drug-induced granulocytopenia, comprising an oligonucleotide as described in claim 9 serving as a primer or probe for detecting a polymorphism of the human insulin receptor substrate-2 gene.

[12] A kit as described in claim 11, which comprises oligonucleotides as described in claim 10.

[13] A kit as described in claim 11, which comprises the oligonucleotides as described in (e) of claim 9 and the restriction enzyme *Afa* I, the kit being employed for detecting A to G conversion at position 29,793 downstream from the translation initiation codon of the human insulin receptor substrate-2 gene.

[14] A method as described in claim 1, which determines the risk of drug-induced granulocytopenia attributed to vesnarinone administration by use of oligonucleotides as described in claim

9 or 10.

[15] A method as described in claim 1, which assesses the risk of drug-induced granulocytopenia attributed to vesnarinone administration by use of the oligonucleotides as described in (e) of claim 9 and the restriction enzyme *Afa* I.

[16] A kit for detecting a polymorphism of the human insulin receptor substrate-2 gene employed for determining the presence of the risk of drug-induced granulocytopenia, the kit comprising oligonucleotides as described in claim 9 as primers or probes for detecting the insulin receptor substrate-2 gene polymorphisms.

[17] A kit as described in claim 16, which comprises oligonucleotides as described in claim 10.

[18] A kit as described in claim 16, which comprises the oligonucleotides as described in (e) of claim 9 and the restriction enzyme *Afa* I, the kit being employed for detecting A to G conversion at position 29,793 downstream from the translation initiation codon of the human insulin receptor substrate-2 gene.

[19] A method as described in claim 2, which detects a genetic polymorphism employed for assessing the risk of drug-induced granulocytopenia attributed to vesnarinone administration by use of oligonucleotides as described in claim 9 or 10.

[20] A method as described in claim 2, which detects a genetic polymorphism employed for assessing the risk of drug-induced granulocytopenia attributed to vesnarinone administration by use of the oligonucleotides as described in (e) of claim 9 and the restriction enzyme *Afa* I.

[21] A method as described in claim 3, in which the examination is carried out concerning the risk of drug-induced granulocytopenia attributed to vesnarinone administration, by use of oligonucleotides as described in claim 9 or 10.

[22] A method as described in claim 3, in which the examination is carried out concerning the risk of drug-induced agranulocytosis attributed to vesnarinone administration, by use of the oligonucleotides as described in (e) of claim 9 and the restriction enzyme *Afa* I.